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Pathologic Fracture Secondary to Subungual Melanoma

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Subungual melanoma is uncommon, and delays in diagnosis and misdiagnosis occur frequently. We describe a 61-year-old black male who presented with a non-healing area in his left thumb nailbed with many of the features of subungual melanoma. However, the patient also had a pathologic fracture of the distal phalanx, leading to some initial confusion about the diagnosis. Despite aggressive multimodality therapy, the disease rapidly progressed, resulting in the patient's death. Pathologic fracture due to subungual melanoma may indicate a particularly poor prognosis.

KEY WORDS: **acrolentiginous melanoma, trauma, wedge biopsy**

INTRODUCTION

Subungual melanomas are uncommon, frequently misdiagnosed neoplasms that were first described in 1866 by Sir Jonathan Hutchinson [1]. They comprise 1.6–3.5% of all cutaneous melanomas [2–4]. Although melanomas are overall much less common in people with dark complexions, the subungual location is noted more frequently in such individuals, occurring in 8–22% of black, Japanese, Hawaiian, and Hispanic melanoma patients [5]. The rarity of this lesion leads to misdiagnosis and delay in diagnosis, making clinical management more difficult and potentially contributing to a worse outcome.

Subungual melanomas may present in a variety of fashions. The majority begin as a brown-black discolored linear streak in the nailbed. Often thickening, splitting, or destruction of the nailplate then follows. In the later stages, common presenting symptoms are ulceration, infection, pain, and bleeding of the nailbed. In 20% [6] to 33% [7] of the cases, the lesions are amelanotic and have an appearance similar to paronychia. Unfortunately, patients with subungual melanomas frequently present late. In this case, the patient presented with several classic features, but in addition had the unusual finding of a pathologic fracture of the distal phalanx secondary to invasive subungual melanoma.

CASE REPORT

A 61-year-old black male presented to the dermatology clinic of Langley Air Force Base in November 1991 with complaints of tenderness and swelling of his dominant left thumb of 6 months duration. He also complained of a nonhealing area in the nailbed with occasional discharge. The patient denied any recent trauma but gave a history of injuring his left thumb 12 years previously. The injury resulted in a dark area underneath his nail, which persisted over the years. Approximately a year prior to presentation, the nail itself came off. The patient had no other complaints.

On physical examination, the distal left thumb was edematous and violaceous. No nail plate existed, and the entire nailbed was covered by a variegated black nodule with slightly purulent drainage. Pigmentation of the periungual tissue (Hutchinson's sign) was present on the ulnar aspect of the lateral nail fold (Fig. 1). Two lymph nodes were palpated in the left axilla. No other suspicious cutaneous lesions were noted, and there was no evidence of organomegaly. A chest X-ray was negative. A radio-

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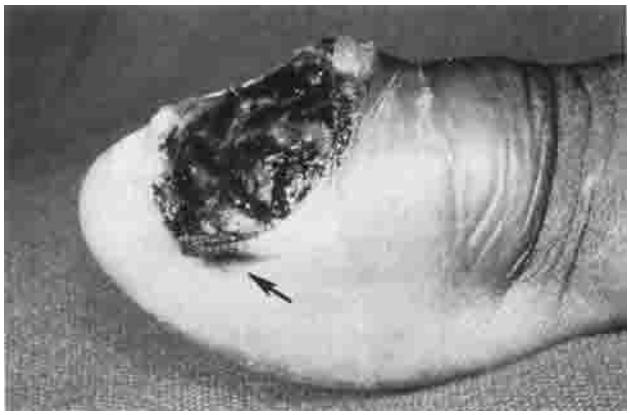

Fig. 1. Photograph of left thumb, demonstrating replacement of left nailbed with a variegated black nodule. Pigmentation of the periungual tissue, known as Hutchinson's sign, is demonstrated (arrow).

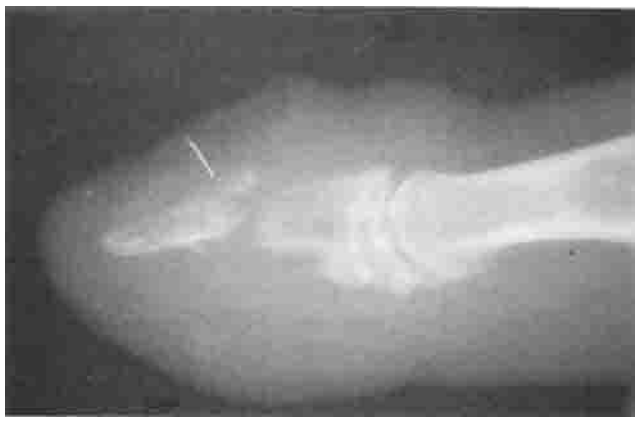

Fig. 2. Plain radiograph of the left thumb reveals a fracture of the distal phalanx.

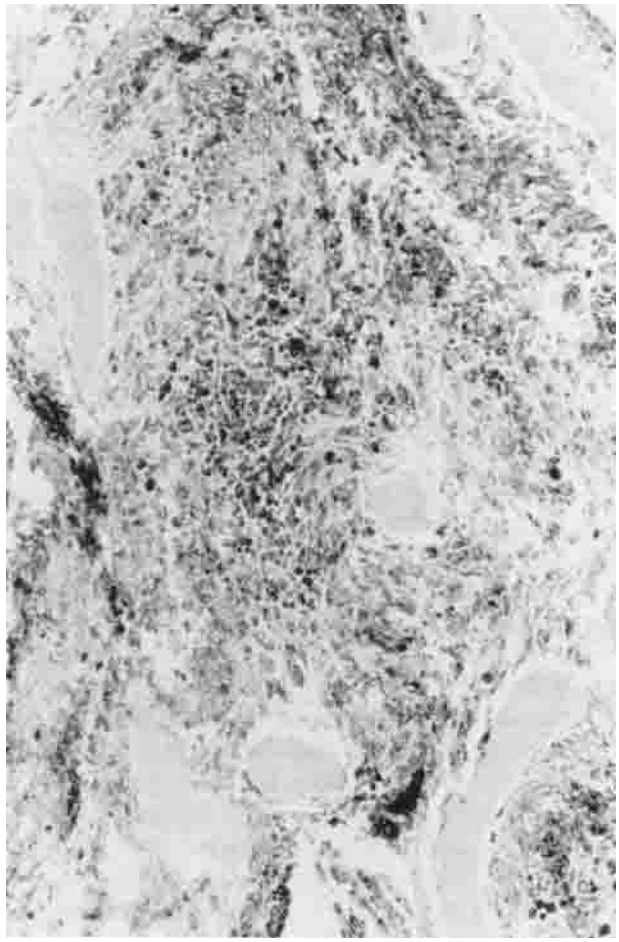

Fig. 3. Histologic section reveals extensive melanocytic proliferation infiltrating the medullary cavity of the phalanx.

graph of the left thumb revealed a fracture of the distal phalanx (Fig. 2).

Melanoma was suspected, and the patient was referred to a surgeon for biopsy. The patient did not go for the biopsy and instead sought care elsewhere. Another surgeon performed a distal amputation of the thumb for presumed osteomyelitis in November 1991. The histopathology revealed a melanocytic proliferation ulcerating the cutaneous surface and invading the periosteum of the distal phalanx with extensive medullary cavity infiltration (Fig. 3) resulting in a pathologic fracture.

At this point, the patient was referred to Eastern Virginia Medical School. On repeat physical examination, there was a small black area consistent with recurrent melanoma at the amputation site. There were also two subcutaneous nodules on the forearm, and the patient's left axillary adenopathy had increased in size. CT scans of the chest and brain were obtained and were significant only for large left axillary lymph nodes. The patient underwent a partial reamputation of his left thumb and biopsy of one of the subcutaneous nodules in February 1992. Both proved to be melanoma on histopathology.

The patient was seen by a multidisciplinary team, and a variety of treatment options were discussed. The patient was treated on a National Biotherapy Study Group protocol consisting of BCNU, cis-platinum, DTIC, tamoxifen, and alpha interferon. Unfortunately, he failed to respond to this regimen and developed more in-transit metastases of his left forearm. In May 1992, the patient elected to undergo left axillary dissection with hyperthermic limb perfusion in an attempt to achieve local control. He received cis-platinum (75 mg/m^2) for 1 hour at 40°C. The patient did well postoperatively and initially showed partial regression of his lesions, but within a 2–3-month period regrowth was apparent.

The patient was then referred to the National Cancer Institute. Attempts to grow tumor-infiltrating lymphocytes failed, and the patient was eventually placed on an interleukin-6 phase I study, to which he did not respond. The patient finally developed systemic disease early in 1993 and died on May 31, 1993, with brain, liver, and lung metastases.

DISCUSSION

This patient's age, race, and primary site of involvement are typical of those with subungual melanoma. What is unusual is the development of a pathologic fracture. Subungual melanomas are equally distributed between men and women and are most commonly seen in patients aged 50–70 years [8]. Blacks and other dark complected individuals have a greater propensity for the disease. The thumb and great toe are the most frequent sites [7–10].

Another typical aspect of this case is the history of trauma to the affected digit. This patient relates that he injured his left thumb 12 years prior to presentation with a resulting dark spot underneath his nail that had persisted since that time. This type of history is commonly elicited from patients with subungual melanoma. Studies have shown a 29–44% incidence of prior trauma to the involved digit with the trauma having occurred anywhere in time up to 20 years prior to presentation [7,11–15]. Although it has been suggested that trauma is actually a direct cause of subungual melanoma [16,17], the majority of the literature does not support a causal link [6,10, 18].

The history of trauma often results in a delay in the patient presenting to a physician since the patient attributes the nailbed changes to the trauma. Even after presenting to the physician, misdiagnosis of subungual melanoma is common. Frequently, 2–3 years pass between the time the patient first notices the lesion and it is accurately diagnosed [8,18]. The varied appearance of subungual melanoma and its rarity contribute to the problem of diagnosis. Other lesions for which it is mistaken include subungual hematoma, paronychia, pyogenic granuloma, onychomycosis nigricans, glomus tumor, benign nevus, subungual exostosis, mucous cyst, subungual fibroma, keratoacanthoma, subungual squamous cell carcinoma, pigmented basal cell carcinoma, osteomyelitis, Bowen's disease, Kaposi's sarcoma, angiosarcoma, and dermatofibroma [7].

The 5-year survival rate for patients with subungual melanoma ranges from 16–53% [3,4,9,10,13]. Although the overall prognosis is poor, survival rates might improve with earlier diagnosis and treatment. To achieve early diagnosis, there must be a high index of suspicion. If a nailbed lesion persists for 4–6 weeks without improvement with conservative treatment, it should be biopsied [8,19]. To ensure a representative sample of both the radial and vertical growth phases, removal of the nail with a wedge biopsy from the area of maximal concern extending to include normal tissue is recommended [19].

Common prognostic factors mentioned in the literature are depth of invasion, thickness, nodal involvement, and distant metastases. Depth of invasion appears to be the *most important indicator* of prognosis [6,10,18]. Due to the unique micro-anatomy of the nailbeds with a thick, hard dermis adherent to underlying periosteum, assessment of the depth of invasion or Clark's level can be difficult [7,9,18,20]. It has been suggested that Clark's level V, which typically refers to invasion into the subcutaneous fat, be modified in subungual melanomas to refer to invasion into the underlying bone since subcutaneous fat is often absent [9]. Gender also may be important since the majority of long-term survivors are women [5, 9,17]. Mitotic rate is also predictive, with a decrease in survival noted with an increase in number of mitotic figures per 10 high power field [20]. A recent multivariate analysis identified stage and S-phase fraction as independent prognostic factors [21]. The literature sometimes refers to advanced cases of subungual melanoma with invasion into bone and notes this as a grave sign [3,7,10, 13,18,21]. Tumor involvement of the highly vascularized medullary cavity may increase the likelihood of metastatic spread. In this case, not only did the subungual melanoma invade bone, but it resulted in a pathologic fracture. This was initially interpreted as osteomyelitis by at least one physician. The poor outcome in this case, despite particularly aggressive therapy, suggests pathologic fracture to be an ominous finding. In reviewing the literature, no other instances of a pathologic fracture secondary to invasive subungual melanoma were found.

Many aspects of treating subungual melanoma are controversial. One aspect of treatment that is agreed upon and was actually first proposed by Hutchinson [1] is early amputation. For lesions of the digits, it is important to preserve length if possible to maximize function. Small lesions confined to the thumb nailbed may be treated with amputation proximal to the distal joint. For more extensive lesions, metacarpophalangeal or metatarsophalangeal amputation are commonly recommended and are reported to have a lower recurrence rate than more distal amputation [7,8,10,19]. A recent study shows that as long as negative margins are achieved, conservative levels of amputation are safe and do not adversely affect local recurrence or survival [21]. In general, lymph node dissection is recommended for patients with clinically positive nodes. Its role, however, in clinically node negative patients remains controversial [6,7,21].

Systemic chemotherapy is often employed in treating subungual melanoma but has not clearly been shown to be of benefit [3,7]. Isolated hyperthermic limb perfusion also has been studied. Muchmore et al. [5] claim that isolated limb perfusion provides a 15–35% increase in survival for patients with advanced subungual melanoma. Baas et al. [10] and Heaton et al. [21], however, showed that although limb perfusion improved locoregional control, it does not improve survival. At this time, there is insufficient data to make any definitive statement on optimal treatment. Randomized prospective trials, although difficult to perform when dealing with low numbers, would be of great benefit in determining the best

method of managing patients with subungual melanoma. For now, it appears the best option for improving outcome is early diagnosis.

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